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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/306,986	05/07/1999	THUAN QUOC TRINH	0942.4570001	4261

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STERNE KESSLER GOLDSTEIN & FOX PLLC
ATTORNEYS AT LAW
1100 NEW YORK AVENUE NW SUITE 600
WASHINGTON, DC 200053934

EXAMINER

HUTSON, RICHARD G

ART UNIT	PAPER NUMBER
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1652

DATE MAILED: 11/05/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/306,986

Applicant(s)

TRINH ET AL.

Examiner

Richard G. Hutson

Art Unit

1652

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 08 September 2004.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 8-13, 56 and 70-75 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 8-13, 56 and 70-75 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| Paper No(s)/Mail Date. _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114.

Applicant's submission filed on 9/8/2004 has been entered.

Applicants amendment of claims 8, in the paper of 9/8/2004, is acknowledged. Claims 8-13, 56 and 70-75 are at issue and are present for examination. Applicants' arguments filed on 9/8/2004, have been fully considered and are deemed to be persuasive to overcome some of the rejections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 8-13 and 71-73 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a

way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 8, 9, 10, 13 and 71-73 are rejected under 35 U.S.C. 112, first paragraph, because the newly added limitation of claim 8 which recites "thereby degrading single-stranded RNA in said preparation" is not supported by the original specification at the time of filing and thus considered new matter. While applicants literal support for the digestion of single stranded RNA is acknowledged applicants newly claimed genus drawn to those methods for synthesizing a nucleic acid molecule comprising the degradation of single-stranded RNA to the exclusivity of RNA in general is considered new matter as applicants do not have support for this claimed sub-genus of methods.

Claim Rejections - 35 USC § 102

The rejection of claims 8, 9, 10, 13 and 71-73 under 35 U.S.C. 102(b) as being anticipated by Davey et al. (U.S. Patent No: 5,409,818, issued 4/25/1995) is hereby withdrawn based on applicants amendment of the claims, specifically claim 8 to include an active step of "degrading single-stranded RNA in said preparation" (See also above 112 1st paragraph rejection), as Davey et al. specifically teach that the ribonuclease of their taught invention "not be capable of hydrolyzing single stranded ...RNA".

The rejection of claims 8, 9, 10, 13, and 72 under 35 U.S.C. 102(e) as being anticipated by Kenten et al. (U.S. Patent No: 6,048,687, filed 6/7/1995) is

hereby withdrawn based on applicants amendment of the claims, specifically claim 8 to include an active step of "degrading single-stranded RNA in said preparation" (See also above 112 1st paragraph rejection), as Kenten et al. specifically teach that the ribonuclease of their taught invention "not be capable of hydrolyzing single stranded ...RNA".

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 8-12, 70, 71 and 73 under 35 U.S.C. 103(a) remain rejected as being unpatentable over Major (Biotechniques, Vol 12, No. 1, 1992, pages 40-43) and Maudru et al. (Journal of Virological Methods 66: 247-261, July 1997).

The rejection was stated in the previous office actions. In response to this rejection applicants have amended claim 8 and traverse the rejection as it applies to the newly amended claims.

Applicants continue to traverse the current rejection on the following basis. Applicants refer to the statements in the previous office action.

While Major does not attribute background difficulties to contaminating RNA, one of skill in the art would realize that given the employment of the method of Major to bacterial lysates, there would be a substantial amount of background RNA in the preparation. This knowledge in combination with that taught by Maudru et al. stating that the background signal in a similar assay was found to be due to an intrinsic

RNA-dependent DNA polymerase activity of the *Taq* DNA polymerase would lead one of skill in the art who was attempting to successfully use a PCR method to screen for small mutations to include a ribonuclease digestion step prior to PCR amplification as a means of making the assay more sensitive. In support of the above, applicants attention is drawn to Major, page 42, middle column, which states "the present results indicate that all three possible terminal T mismatches can be equally discriminated under standard PCR conditions, **especially** when using mini-prep DNA". Such a statement clearly supports that even Major recognized the taught method had different results or sensitivities depending on the template used (noting the reference to "especially"), although Major did not comment on the specific difference of the two different types of template preparations. One of skill in the art would understand that the difference was likely the presence of contaminating material, such as RNA.

In response to the above applicants submit that the above reasoning is both logically and technically flawed based on the following:

First applicants submit that a bacterial lysate contains many factors besides RNA (e.g., proteins, salts, lipids, signaling molecules, etc.) and that these other factors are absent from mini-prep DNA, and thus there is no reason why one of ordinary skill in the art would have specifically regarded RNA as the one factor responsible for the difference in 3'-terminal mismatch discrimination alluded to in Major. Applicants submit that the only such evidence is presented in applicants own specification, which can not be used against applicants. This first point has been considered in full, however found non-persuasive. As previously stated in the original rejection,

"Maudru et al. teach that the background signal of the PCR-based reverse transcriptase assay is due to an intrinsic **RNA-dependent** DNA polymerase activity of the *Taq* DNA polymerase enzyme and they teach that this background

signal could be eliminated by the addition of a ribonuclease to the amplification reaction".

This previously presented evidence as taught by Maudru, is in part the basis of the conclusion of the components present in a bacterial lysate relative to a mini-prep, it is the RNA which is most likely the source of interference.

Applicants continue to traverse the rejection on the basis that the second flaw in the rejection is the implication that a person of ordinary skill in the art would have believed that errors in terminal nucleotide mismatch discrimination occur only in bacterial colony lysates (which contain RNA) but not in other DNA preparations (which do not contain RNA). Applicants submit that it was well known in the art at the time of the effective filing date of the application that errors in terminal mismatch discrimination occurred in purified DNA preparations, and applicants present Kwok et al. in support of this specific assertion.

Applicants comments are acknowledged, however, while it is appreciated that "errors in terminal mismatch discrimination occurred in purified DNA preparations", the comment by Major, which lead to the implications applicants refer to is based on the above repeated recitation from Major which states:

"the present results indicate that all three possible terminal T mismatches can be equally discriminated under standard PCR conditions, **especially** when using mini-prep DNA". As previously stated, such a statement clearly supports that even Major recognized the taught method had different results or sensitivities depending on the template used (noting the reference to "especially"), although Major did not comment on the specific difference of the

two different types of template preparations. The only templates used by Major were mini-prep DNA and bacterial lysates, and thus the "especially" is in reference to these two different templates only. It is recognized that errors in terminal mismatch discrimination occurred in purified DNA preparations, this is not in dispute nor is this the point of the previously recited comments by Major. Thus applicants submitted flaw in the rejection is also not found persuasive.

Finally applicants assert that a person of ordinary skill in the art would not have had any motivation to combine Maudru with Major as the references deal with entirely different non-analogous assay systems. Applicants argument is acknowledged, however found nonpersuasive, because the basis to combine the References is as previously stated, based on the fact that both references teach methods of amplification of nucleic acids. Applicants characterization of Maudru as being concerned with assaying the presence of reverse transcriptase in a sample is misleading. In support applicants attention is directed to the title of Maudru which is "Elimination of background signals in a modified polymerase chain reaction-based reverse transcriptase assay".

Applicants complete argument is acknowledged, however continues to be found non-persuasive and the rejection of claims 8-12, 70, 71 and 73 is maintained.

Remarks

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Richard G Hutson whose telephone number is (571) 272-0930. The examiner can normally be reached on 7:30 am to 4:00 pm, M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy can be reached on (571) 272-0928. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

A handwritten signature in black ink, appearing to read 'Richard G. Hutson', with a stylized flourish at the end.

Richard G Hutson, Ph.D.
Primary Examiner
Art Unit 1652